RT 127

Pharmacology

Pharmacokinetics of Inhaled Drugs

Administration:

Topical effect on upper and lower airways - respiratory drugs

Systemic effect via absorption and distribution in blood - insulin, antivirals, etc.

A certain amount of aerosolized drug will always impact in the naso- or oropharynx and be swallowed. Efforts are made through improvement in delivery devices and patient breathing technique to maximize the amount of drug delivered to the lungs. It is a most imprecise way of delivering medication - yet due to its topical delivery it allows the administration of a much smaller dose to achieve the desired effect.

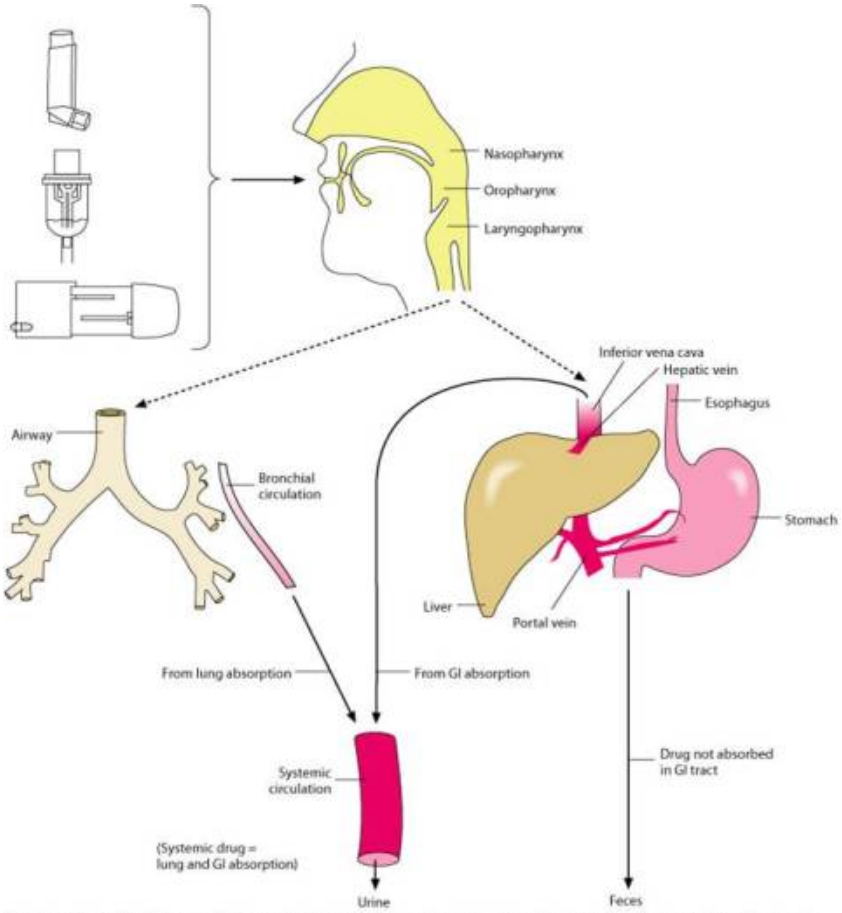


Fig. 2-6. Orally inhaled aerosol drugs distribute to the respiratory tract and to the stomach through swallowing of oropharyngeally deposited drug. *Top left*: The inhalation devices shown include a metered dose inhaler *(top)*, a nebulizer *(middle)*, and a dry powder inhaler *(bottom)*. *GI*, Gastrointestinal.

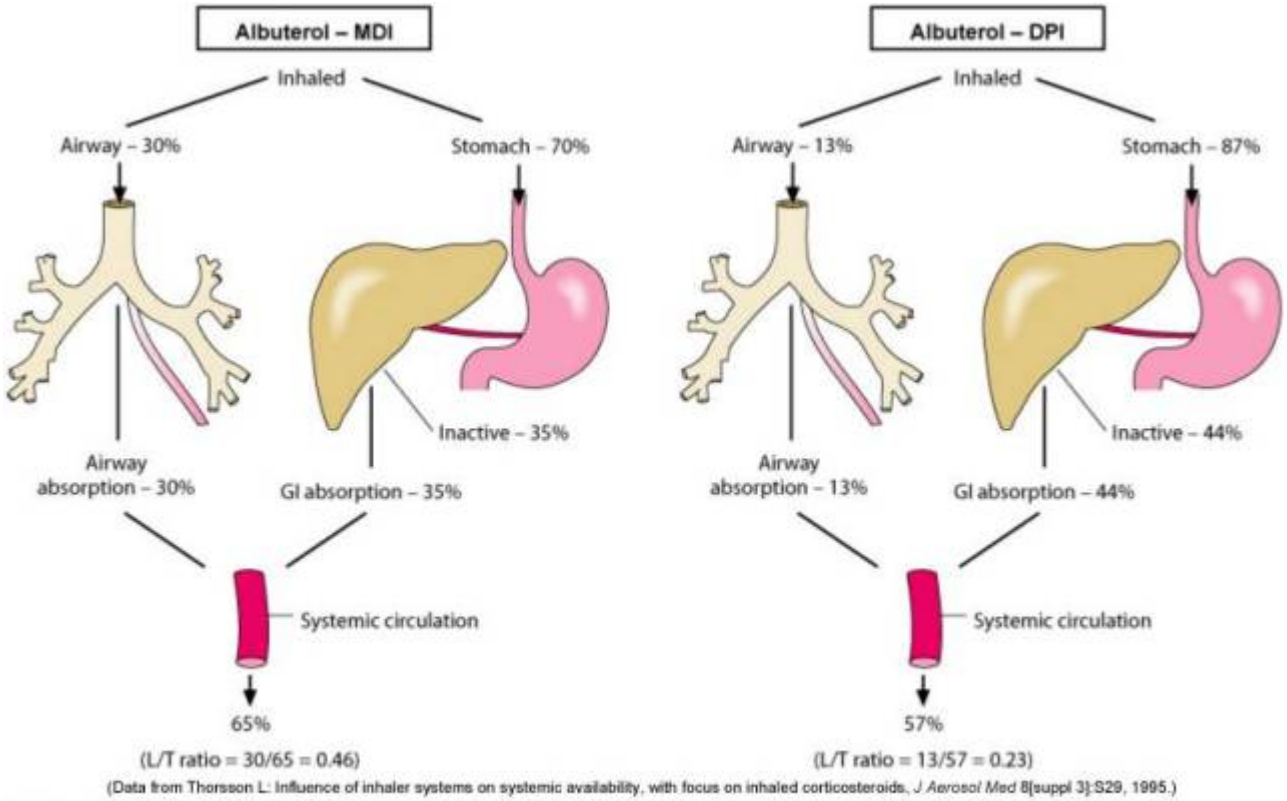
Topical Tx: COPD, CF, Asthma

Goal - To maximize lung deposition / minimize systemic exposure and unwanted side effects

High lung availability/Total systemic availability

L / T Ratio

- Proportion of drug available from the lung, out of the total systemically available drug
- Formula: (Lung dose)/(lung dose + GI dose)
- ***The higher the ratio the more efficient the aerosol drug delivery to the respiratory tract***



(Data from Thorsson L: Influence of inhaler systems on systemic availability, with focus on inhaled corticosteroids, *J Aerosol Med* 8[suppl 3]:S29, 1995.)

Fig. 2-7. The lung availability/total systemic availability (L/T) ratio can quantify the efficiency of aerosol drug delivery to the respiratory tract by partitioning relative amounts from the gastrointestinal tract and from the respiratory tract (see text for explanation).

The Box 2-4 below gives techniques that can increase delivery to the lung or decrease systemic availability - the first and fourth factor increase delivery of drug to the lung while aiming to reduce oropharyngeal deposition and swallowing. The second factor addresses the amount of drug that is swallowed but metabolized quickly. The third suggestion, while not preventing oropharyngeal deposition, minimizes amount of drug that is swallowed by physically eliminating by rinsing and spitting. You will see staff have the patient rinse and swallow - and while this is a good way to prevent oral thrush as a result of inhaled steroids it does add to the systemic availability of the drug. I recommend doing both - first have the patient rinse and spit, then have the patient rinse and swallow as this will also clear the back of the throat and pharyx that is not reached when the patient only rinsing the oral cavity and spits.

Box 2-4 Factors Increasing the Lung Availability/Total Systemic Availability (L/T) Ratio With Inhaled Drugs

- Efficient delivery devices (high airway and low gastrointestinal delivery)
- Inhaled drugs with high first-pass metabolism
- Mouthwashing, including rinsing and spitting
- Use of a reservoir device (spacer, holding chamber) to decrease oropharyngeal deposition and swallowed drug amount

Please note the differenec in the table below between the good coordinators and the poor coordinators for the pMDI - pressurized metered dose inhaler - the most common method of self-medication for patients with breathing problems. Poor coordination means not coordinating the dispensing of the dose with a properly timed inhalation - this often is a result of improper instruction in how to take the MDI. One of the most important roles you will have as a RCP is that of patient education!

TABLE 2-5

Lung Availability/Total Systemic Availability (L/T) Ratios for Several Inhaled Drugs With Various Aerosol Delivery Devices*

Drug	Device	Lung Deposition (%)	L/T Ratio	Subjects
Albuterol	pMDI	18.6	0.36	Patients—good coordinators
		7.2	0.17	Patients—poor coordinators
	BAI (pMDI)	20.8	0.41	Patients—poor coordinators
	Turbuhaler	23.2	0.45	Healthy volunteers
Budesonide	pMDI (CFC)	15.0	0.66	Healthy subjects
	Turbuhaler	32.0	0.87	Healthy subjects
	MDI (HFA)†	59.0	0.92	Patients

Data from Borgström L: Local versus total systemic bioavailability as a means to compare different inhaled formulations of the same substance, *J Aerosol Med* 11:55, 1998.
BAI, Breath-actuated inhaler; *CFC*, chlorofluorocarbon; *HFA*, hydrofluoroalkane; *pMDI*, pressurized metered dose inhaler.
*All drug amounts are expressed as percentages of metered or nominal dose.
†Harrison LI: Local versus total systemic bioavailability of beclomethasone dipropionate CFC and HFA metered dose inhaler formulations, *J Aerosol Med* 15:401, 2002 [erratum in: *J Aerosol Med* 2003;16:97].